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| 10/613,106 | 07/03/2003 | Yuanhao Li | CELL-026 | 6569 |

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| EXAMINER | |
|---|---|
| GUZO, DAVID | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | |

DATE MAILED: 03/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/613,106 | LI ET AL. | |
| | Examiner | Art Unit | |
| | David Guzo | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 July 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/5/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## Detailed Action

### 35 USC 102 Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4-5, 9, 12, 14, 17, 19 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Gao et al.

Applicants claim an adenovirus packaging cell line permissive for replication of an EIA/EIB deficient adenovirus vector, wherein said cell line comprises an adenovirus EIA coding sequence and an adenovirus EIB coding sequence operably linked to a promoter (which can be a constitutive promoter) that lacks substantial sequence identity with a native adenovirus EIA or EIB promoter. The E1a and E1b sequences can be stably integrated into the genome of the cell, the E1a and E1b coding sequences can be operably linked to the same or different promoters and the E1a and E1b sequences encode the different gene products (i.e. the 243 and/or 289 gene products of E1a, etc.). Applicants also claim a method of producing an adenovirus packaging cell line comprising introducing into a cell line permissive for adenovirus replication an expression vector comprising the aforementioned E1a and E1b sequences and promoters as well as a method of producing E1a/E1b deficient adenoviruses comprising introducing a E1 deficient adenovirus into the above mentioned cell line.

It is noted that applicants recite that two nucleic acids are "operably linked" (on p. 10 of the specification) when one nucleic acid is placed into a functional relationship with the other nucleic acid. Applicants further indicate that a promoter is operably linked to a coding sequence if it affects the transcription of the sequence. It is also noted that expression of E1a regulates the expression of E1b during adenovirus infection. By this definition a heterologous promoter controlling expression of the E1a coding sequence is also operably linked to the E1b coding sequence because the expression of E1a by the heterologous promoter regulates expression (transcription) of the E1b sequences by the E1b promoter. With regard to claims 12 and 14, it is noted that the specific gene products cited are the normal gene products produced from intact E1a and E1b coding regions.

Gao et al. (cited by applicants, see whole article, particularly the Abstract, the paragraph bridging pp. 213-214, the paragraph bridging pp. 214-215 and the first six paragraphs in the "Results and Discussion" section on pp. 217-218) recites an adenovirus packaging cell line (GH329) permissive for replication of an EIA/EIB deficient adenovirus vector, wherein said cell line comprises an adenovirus EIA coding sequence and an adenovirus EIB coding sequence wherein the E1a coding region is operably linked to the constitutive promoter from the phosphoglycerate kinase gene (PGK) wherein said PGK promoter lacks substantial sequence identity with a native adenovirus EIA or EIB promoter. Given applicants definition of "operably linked" (see above), it must be considered that the E1b coding region is also operably linked to the PGK promoter since expression the E1a gene products regulates expression of the E1b

coding sequence. The E1a and E1b sequences can be stably integrated into the genome of GH329 cells, and since the entire 3.4 kb E1 (E1a and E1b) fragment was used to generate the GH329 cells, it must be assumed, absent evidence to the contrary, that all of the gene products normally encoded by E1a and E1b are present (i.e. the 243 and/or 289 gene products of E1a, and the 19 and 55 kd gene products of E1b). Gao et al. also claim a method of producing an adenovirus packaging cell line comprising introducing into a cell line permissive for adenovirus replication an expression vector comprising the aforementioned E1a and E1b sequences and promoters as well as a method of producing E1a/E1b deficient adenoviruses comprising introducing a E1 deficient adenovirus into the above mentioned cell line. With regard to the instant rejection being applied to both claims 4 **and** 5, the PGK can be considered to be operably linked to both the E1a and E1b coding sequences and hence the E1a and E1b sequence are operably linked to the same promoter. On the other hand, the E1a and E1b are operably linked to different promoters in that the PGK promoter is operably linked to the E1a coding sequence and the E1b promoter is operably linked to the E1b coding sequence. In this context, the E1b coding sequence can be considered to be operably linked to both or either of the PGK and/or E1b promoters. Finally, Gao et al. indicates that multiple copies of the E1 vector appear to be integrated into the cellular genome, but it cannot be determined if the copies are integrated in tandem or at different sites in the genome. Gao et al. therefore teaches the claimed invention.

Claims 1-2, 4-5, 9-10, 12, 14, 17, 19 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Imler et al.

Applicants' invention is as described above. Additionally, claim 10 recites that the promoter that lacks substantial identity with a native adenovirus E1a or E1b promoter is a regulatable promoter.

Imler et al. (US 2001/0049136, published 12/6/2001, see whole document, particularly Fig. 6; paragraphs [0037]; [0079]; [0088]; [0089]; [0095]; [0100]-[0107]; [0206]; [0215]; claims 32-45) teaches adenovirus packaging cell lines (derived from BHK or A549 or Vero cells, etc.) permissive for replication of an EIA/EIB deficient adenovirus vector, wherein said cell line comprises an adenovirus EIA coding sequence and an adenovirus EIB coding sequence wherein the E1a coding region is operably linked to a constitutive promoter (such as the phosphoglycerate kinase gene (PGK)) or a regulatable promoter (such as a promoter inducible by the *Saccharomyces cerevisiae* Ga14 protein) wherein said promoters lack substantial sequence identity with a native adenovirus EIA or EIB promoter. Given applicants definition of "operably linked" (see above), it must be considered that the E1b coding region is also operably linked to the PGK promoter since expression the E1a gene products regulates expression of the E1b coding sequence. The E1a and E1b sequences can be stably integrated into the genome of the packaging cells, and since the entire E1 (E1a and E1b) fragment was used to generate the packaging cells, it must be assumed, absent evidence to the contrary, that all of the gene products normally encoded by E1a and E1b are present (i.e. the 243 and/or 289 gene products of E1a, and the 19 and 55 kd gene products of

E1b). Imler et al. also claim a method of producing an adenovirus packaging cell line comprising introducing into a cell line permissive for adenovirus replication an expression vector comprising the aforementioned E1a and E1b sequences and promoters as well as a method of producing E1a/E1b deficient adenoviruses comprising introducing a E1 deficient adenovirus into the above mentioned cell line. Imler et al. therefore teaches the claimed invention.

## 35 USC 101 (Double Patenting) Rejections

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-23 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-23 of copending Application No. 10/857,137. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

## 35 USC 112, 2nd Paragraph Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 20-22 are vague in that there is no antecedent basis for the terms "said E1A expression vector" or "said E1B expression vector" or "said E1A and E1B expression vectors" in claim 17.

**Claim Objections**

Claims 18-19 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 18 does not further limit claim 17 fore the following reason. Claim 17 recites a method for producing an adenovirus packaging cell line comprising introducing into the cell line "**an** (emphasis added) expression vector" comprising the E1A and E1B coding sequences operably linked to promoters. However, claim 18 recites that the E1A and E1B coding sequences are present on **separate** vectors and therefore claim 18 does not further limit claim 17.

Claim 19 recites that the E1A and E1B coding sequences are present on **the same** vector and therefore claim 18 does not further limit claim 17 because claim 17 recites that the E1A and E1B sequences are present on "**an expression vector**". Both claim 17 and 19 recite that the E1A and E1B sequences are present on a single vector.

No Claims are allowed.

Claims 3, 6-8, 11, 13, 15, 16 and 18 are free of the art because said art does not teach adenoviral packaging cell lines comprising separate stably integrated vectors encoding E1a on one vector and E1b on a second vector wherein the E1a and E1b sequences are under control of different non-adenoviral promoters. Also, the prior art does not teach packaging cells with the E1a and E1b gene operably linked to identical promoters or packaging cells with the E1a and/or E1b genes operably linked to a retroviral promoter or packaging cells with the E1a and e1b sequences integrated at different sites in the cell genome.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Guzo
March 13, 2005